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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/700,293      | 11/13/2000  | Jean-Louis Ruelle    | BM45321             | 3367             |

25308 7590 09/30/2003

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EXAMINER

BASKAR, PADMAVATHI

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1645

DATE MAILED: 09/30/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                     |                    |  |
|------------------------------|---------------------|--------------------|--|
| <b>Office Action Summary</b> | Applicati n No.     | Applicant(s)       |  |
|                              | 09/700,293          | RUELLE, JEAN-LOUIS |  |
|                              | Examiner            | Art Unit           |  |
|                              | Padmavathi v Baskar | 1645               |  |

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 24 June 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 60-70<sup>67</sup> is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 60-70<sup>67</sup> is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                   | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                          | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>11</u> . | 6) <input type="checkbox"/> Other:  |

### **DETAILED ACTION**

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/24/03 has been entered.
2. The amendment filed on 6/24/03 has been entered into the record. Claim 66 has been amended. Claims 60-67 are pending in the application.

#### ***Information Disclosure Statement***

3. Information Disclosure Statement filed on 6/24/03 (Paper # 11) is acknowledged and a signed copy is attached to this Office action.
4. The rejection of claims 60-67 under 35 U.S.C. 102(e) as being anticipated by Peak et al 2001. U.S. Patent 6,197,312 (102 e date is 12/14/1998) is withdrawn as priority is granted as of 5/13/1998 for claims 60-67 with respect to SEQ.ID.NO. 2.

#### ***Claim Rejections - 35 USC 112, first paragraph***

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Art Unit: 1645

6. Claims 60-67 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is referred to the interim guidelines on written description published June 15, 1998 in the Federal Register at Volume 63, Number 114, pp 32639-32645 (also available at [www.uspto.gov](http://www.uspto.gov)). This is a written description rejection.

The claims are drawn to an isolated polypeptide comprising the amino acid sequence SEQ.ID.NO: 2 or 4 and an immunogenic fragment comprises at least 15 amino acids or 20 amino acids. Claims are also drawn to fusion protein and immunogenic composition comprising said fragments, pharmaceutically acceptable carrier and adjuvant.

The specification broadly describes as part of the invention, an isolated protein of SEQ ID NO: 2 or 4, which is encoded by BASB 029 gene from *Neisseria meningitidis* strains ATCC 13090 and H44/76. The specification also teaches that this full-length protein contains 594 or 591 amino acids. However, the specification does not teach fragments or immunogenic composition or fusion protein comprising said fragments (i.e., 15 amino acids or 20 amino acids.)

The actual biological function of the protein represented as SEQ ID NO: 2 or 4 is not set forth in this specification. Applicants broadly describe the invention as embracing any deletion by use of language in which a specified percent of amino acids can be changed in the protein. USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See

Art Unit: 1645

page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116).

Thus, an isolated polypeptide comprising the amino acid sequence SEQ ID NO: 2 or 4 meets the written description provision of 35 U.S.C. 112, first paragraph for the reasons set forth below.

The specification fails to teach an isolated polypeptide fragments of SEQ ID NO: 2 or 4 and it is noted that the claimed fragments do not exist as an invention independent of their function in encoding a protein, SEQ.ID.NO: 2 or 4. The actual structure or other relevant identifying characteristics of each protein fragment having the claimed properties of the protein can only be determined empirically by actually making every nucleic acid that encodes the recited fragments and testing each to determine whether such a fragment having the particularly disclosed properties of full length protein. For example, if there is a well-established correlation between structure and function in the art, one skilled in the art will be able to reasonable predict the complete structure of the claimed invention from its function. This specification does not teach such, and the art is devoid of this correlation for protein SEQ ID NO: 2 or 4with undetermined function. There is no written description support for an isolated fragments comprising 15 amino acids or 20 amino acids or immunogenic composition or fusion protein comprising said fragments as claimed.

The isolated polypeptide comprising of SEQ ID NO: 2 or 4 is uncharacterized by this specification and is not asserted to belong to any known family of proteins. The specification fails to teach the structure or relevant identifying characteristics of a representative number of SEQ.ID.NO: 2 or 4 fragments, sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method

Art Unit: 1645

for isolating it. See *Fiers v. Revel*, 25 U5PQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc V Chugai Pharmaceutical Co Ltd.*, 18 U5PQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 U5PQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

7. Claims 60-67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide comprising the amino acid sequence SEQ ID NO: 2 or 4, fusion protein comprising the amino acid sequence SEQ ID NO: 2 or 4 does not reasonably provide enablement for an isolated polypeptide comprising a fragment of at least 15 or 20 amino acids or immunogenic composition comprising said fragments of SEQ ID NO: 2 or 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

BASB 029 gene from *Neisseria meningitidis* strains ATCC 13090 and H44/76. The specification also teaches that this full-length protein contains 594 or 591 amino acids. The specification discloses the claimed polypeptide could be used as an immunogen (pages 51-58) and formulating the compositions in Freund's adjuvant to immunize mice for preparing antibodies. However, the specification fails to teach an isolated polypeptide comprising a fragment of at least 15 or 20 amino acids or immunogenic composition comprising said fragments of SEQ ID NO: 2 or 4. Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology and the art teaches that the significance of any particular amino acid sequences (i.e. fragments) for different aspects of biological activity cannot be predicted a priori and must be determined empirically on a case-by-case basis (Rudinger et al, in "PEPTIDE HORMONES", edited by Parsons, J.A., University Park Press, June 1976, page

Art Unit: 1645

6). The art specifically teaches that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological-activity of the protein (Burgess et al., *The Journal of Cell Biology*, 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biologic activity of the mitogen (Lazar et al., *Molecular and Cellular Biology*, 8(3): 1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a protein. Proteins with replacement of single amino acid residues may lead to both structural and functional changes in biological activity and immunological recognition. For example, Jobling et al. (*Mol. Microbiol.* 1991, 5(7): 1755-67 teaches a panel of single amino acid substitutions by oligonucleotide directed mutagenesis which produces proteins that differ in native conformation, immunological recognition, binding and toxicity, thus exemplifying the importance of structural components to both biological function and immunological recognition. Applicants have not taught which residues of SEQ ID NO: 2 or 4 can be varied and still achieve a polypeptide that is functional as an immunogenic composition or is capable of use as a diagnostic using immunological means of recognition. The specification has not conceived any other functionally equivalent protein fragment and does not set forth the general tolerance to substitutions and where substitutions could be made. Since, the specification lacks a written description of any fragment of SEQ ID NO: 2 or 4, it is not enabled for this language because it fails to enable the skilled artisan to envision the detailed chemical structure of the claimed polypeptide fragment of SEQ ID NO: 2 or 4 respectively, as well as how to use the polypeptide

Art Unit: 1645

unpredictability of the art, the lack of teachings of the specification, it would require undue experimentation on the part of the skilled artisan to practice the invention as claimed.

***Claim Rejections - 35 USC 112, second paragraph***

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

9. Claims 60-67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 60 is vague and not clear whether the immune response induced by the immunogenic fragment has the ability to bind to an antibody raised against full-length protein. It is suggested that this claim to be amended to recite " An isolated polypeptide -----, wherein the immunogenic fragment when administered----- -- immune response that recognizes the isolated polypeptide SEQ ID NO: 2.

***Claim Rejections - 35 USC 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the

Art Unit: 1645

reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

11. Claims 60-67 with respect to SEQ.ID.NO: 4 are rejected under 35 U.S.C. 102(e) as being anticipated by Peak et al U.S.Patent 6,197,312 (102 e date is 12/14/1998).

Please note that the claims 60-67 with respect to SEQ.ID.NO: 4 get priority date as of 5/7/1999 (see paper # 6).

Claims are directed to an isolated polypeptide comprising an amino acid sequence matching SEQ.ID.NO: 2 or SEQ.ID.NO: 4 and an immunogenic fragment of at least 15 amino acids, fusion protein comprising the same and immunogenic comprising the same.

Peak et al disclose an isolated polypeptide SEQ.ID.NO: 21 comprising an amino acid sequence that contains 591 amino acids that matches with SEQ.ID.NO: 4 (99. 9%) of the claimed invention in column 97-100, claims U.S.Patent 6,197,312 and see the attached sequence alignment. Further, the prior art also discloses immunogenic fragments containing at least 50 amino acids that include 15-20 amino acids of the claimed invention (see claim 5), fusion proteins (see figure 1 and examples 2-4) and immunogenic compositions (see claims 7-10). The prior art anticipated the claimed invention.

#### ***Status of Claims***

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886.

The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Art Unit: 1645

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D.

9/9/03

  
LYNETTE R. F. SMITH  
SUPERVISORY PATENT EXAMINER  
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